REMARKS

Claims 89 and 130-157 are pending. Claim 158 has been canceled and claims 89, 130 and 131 have been amended. Claims 159-173 have been added to more clearly define the invention. Applicants preserve the right to file any canceled or withdrawn subject matter in one or more continuation or divisional applications.

The Examiner has provisionally rejected claims 89 and 130-158 under the judicially created doctrine of obviousness-type double patenting over claims 89 and 130-153 of co-pending Application No. 10/602,976. Applicants enclose a terminal disclaimer to overcome this rejection.

The Examiner's attention is directed to the recent issuance of US Patent Nos. 6,812,219 and 6,914,054, and additional co-owned co-pending U.S. Application Nos. 10/602,135; 10/602,136; 10/602,142; 10/602,691; 10/602,693; and 10/602,694. While not admitting that such is needed, Applicants enclose a terminal disclaimer that disclaims the terminal portion of a patent issuing on this application that would extend beyond the term of these patents or a patent issuing on these listed patent applications.

The Examiner has also objected to claim 158 as improper. The claim has been canceled in response to the Examiner's objection.

Applicants were pleased to note that the Examiner found that the specification was enabling for methods of treatment of flavivirus and pestivirus infections for compounds wherein R^1 and R^2 are H, phosphate, or a stabilized phosphate prodrug; acyl; alkyl; sulfonate ester; or benzyl, R^6 is lower alkyl and R^7 is other than hydrogen. However, the Examiner has rejected claims 89 and 130-158 under 35 U.S.C. § 112, first paragraph because the Examiner alleges that the specification is not enabled for the methods in which the compounds are substituted at R^1 and R^2 with "lipids, amino acids... phosphate," where R^6 is anything other than lower alkyl or R^7 is hydrogen.

The Examiner suggests that the phrase "or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate" is not enabled. Applicants respectfully point out to the Examiner that the R^1 and R^2 substituents are forms of esters, and esters are known to cleave in vivo to free hydroxyl groups through a variety of specific and non-specific esterases. There is abundant literature describing the cleavage of esters from nucleosides in the body. In such a well trodden area, it is late in the day to suggest that the skilled worker would not be able to practice this known art. .

The Examiner also suggests that the specification is not enabling for the scope of the remaining substituents R^1, R^2, R^6 and R^7. Applicants maintain that the specification is fully enabled for uses of the 2'-branched compounds where R^1 or R^2 is a lipid, an amino acid, a carbohydrate, a peptide, or cholesterol. Applicants note that the Examiner has already found that the description of methods of synthesis of 2'-branched nucleosides, for example on pages 62-66, is sufficient to enable the claims for a variety of substituents. Other methods are known in the art. Applicants additionally point to the description on pages 52-53, which describe methods of preparation of lipid prodrugs of the compounds recited in the claims. In addition, page 52 points to other prodrug modifications, such as alkylation, acylation, etc. On pages 64-66, modifications of the 2'-branched nucleoside is described, which can yield a 2'-branched compound including lipids, amino acids, carbohydrates, peptides or cholesterol at R^1 or R^2. The methods described and references discussed in the specification would lead a skilled artisan to preparation of 2'-branched compounds that include these substituents at R^1 or R^2. The patent application also teaches how to use the claimed compounds, for example on pages 55-58, wherein there is a detailed discussion of how to formulate and administer the compounds to a patient in need thereof.

The Examiner has indicated that the specification does not provide examples of the use of compounds with the rejected substituents. However, Applicants note that the specification teaches that lipid, amino acid, peptide and cholesterol substitutions provide *prodrugs* of the

active compounds. The substituents are therefore cleaved *in vivo* and the remaining compound would be the active agent. Furthermore, lipid, amino acid, peptide and cholesterol substitutions are well known in the art and one of skill in the art would expect the compounds to be merely a different form of delivery.

Applicants also maintain that the specification is enabled for R^6 as other than lower alkyl and R^7 as hydrogen. In addition to the description of preparation of the compounds on pages 62-66, there are specific examples of each of these groups provided in the specification. For example, substituents other than lower alkyl for R^6 are described on pages 139-140, which lists specific examples of compounds. In addition, compounds in which R^7 is hydrogen are listed on pages 137-139. The description therefore provides not only methods of preparation, but specific examples of compounds that support the rejected substituents. A skilled artisan would be directed to use compounds with the particular listed substituents in the recited methods.

The Examiner has also rejected these claims under 35 U.S.C. §112, second paragraph as indefinite for the recitation of the phrase "benzyl, wherein the phenyl group is optionally substituted...". Applicants have amended claim 89 to recite substituent groups that are identified in the definition of "aryl" in the specification on page 49 to overcome the Examiner's rejection.

Should the Examiner determine that additional fees are due, the Commissioner is hereby authorized to debit any fees associated with this response to Deposit Account 11-0980.

Respectfully submitted,

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